Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1 and 12 have been amended and claims 6, 17, and 21-26 have been canceled. Support for the amendments to claims 1 and 12 is found in the present application, as filed, at page 5, lines 5-15, and page 29, line 28 through page 30, line 9. Claims 1, 4-5, 7-9, 12, 15-16, and 18-20 are pending. No new matter has been added.

The rejection of claims 1, 4-12, and 15-20 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is respectfully traversed.

As amended, claim 1 is directed to a method of treating Alzheimer's Disease in a subject. This method involves administering to the subject an agent, where the agent (1) binds to a site of apolipoprotein E that binds to SEQ ID NO:4, and (2) inhibits interaction between amyloid-β peptide and apolipoprotein E, compared to when the agent is absent, to treat Alzheimer's Disease in the subject. Amended claim 12 is directed to a method of inhibiting accumulation of amyloid-β peptide deposits in a subject's brain. This method involves administering to the subject an agent, where the agent (1) binds to a site of apolipoprotein E that binds to SEQ ID NO:4, and (2) inhibits interaction between amyloid-β peptide and apolipoprotein E, compared to when the agent is absent, to inhibit accumulation of amyloid-β peptide deposits in the subject's brain.

It is the position of the U.S. Patent and Trademark Office that the present application enables only a method of treating Alzheimer's disease by administration of Aβ12-28P (SEQ ID NO:4). Applicants respectfully disagree.

According to the present application, Aβ12-28P (i.e., SEQ ID NO:4) was administered to AD Tg mice to investigate the *in vivo* effect of blocking the apolipoprotein E/amyloid-β peptide (apoE/Aβ) interaction on amyloid deposition. Present Application, pg. 5, lines 5-7. It was demonstrated that blocking the specific binding site for amyloid-β peptide on apolipoprotein E resulted in the inhibition of formation of amyloid-β peptide deposits in the brain of the transgenic animals. Present Application, at pg. 5, lines 8-9. Accumulation of amyloid-β peptide in the brains of Alzheimer's Disease patients is the hallmark of Alzheimer's Disease pathology. Present Application, at pg. 33, lines 1-2.

The inhibition profile of Aβ12-28P against apolipoprotein E/amyloid-β peptide interaction is set forth in Figure 3 of the present application and, as further described in Example 15, the concentration of an agent producing half-maximal inhibition (IC_{50}) can be

calculated from a non-linear regression, one-site competition curve. Present Application, at pg. 29, line 31 through pg. 30, line 2. In the case of Aβ12-28P, the inhibition constant was calculated to be 11.37 nmol given the known dissociation constant of Aβ1-40 binding to apolipoprotein E (i.e., approximately 10 nmol). *Id.* Furthermore, inhibition of the apolipoprotein E/amyloid-β peptide interaction at the site on apolipoprotein E which binds to Aβ12-28P appears to be nontoxic, because it does not inhibit any physiological reaction (like blocking amyloid β secretase, which serves multiple functions) and does not cause an autoimmune response (like the vaccine whose phase II clinical trial was stopped due to morbidity and mortality). Present Application, at pg. 5, lines 8-15.

With this guidance, a person of ordinary skill in the art can develop other agents, such as proteins or peptidomimetics, non-proteinaceous agents, and modified proteins, using well known techniques, as set forth in the present application. Present Application, at pgs. 8, line 1 through pg. 13, line 17. In addition, the competitive inhibition assay described in Example 5 of the present application can be used to identify agents that (1) bind to a site of apolipoprotein E that binds to Aβ12-28P and (2) inhibits interaction between amyloid-β peptide and apolipoprotein E.

Faced with all of this information, it is submitted that a person of ordinary skill in the art would be fully able to carry out the methods set forth in the present claims. Accordingly, the rejection of claims 1, 4-12, and 15-20 for lack of enablement is improper and should be withdrawn.

The rejection of claims 6 and 17 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is obviated by the above cancellation of these claims.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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